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Elan Drug Delivery, Inc. c/o Foley & Lardner
3000 K Street, N.W.
Suite 500
Washington, DC 20007-5109

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HOLT, ANDRIAE M	

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/768,194
Filing Date: February 02, 2004
Appellant(s): HOVEY ET AL.

Michelle M. Simkin
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed April 5, 2010 appealing from the Office action mailed November 5, 2009.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The following are the related appeals, interferences, and judicial proceedings known to the examiner which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal:

U. S. Application Serial No. 10/035,324 is a related appeal.

(3) Status of Claims

The following is a list of claims that are rejected and pending in the application:

Pending claims 17, 19-24, 27-44, 47-61, 64-67, and 69-81 are finally rejected.

(4) Status of Amendments After Final

The appellant's statement of the status of the amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

5,747,001	Wiedmann et al.	5-1998
6,241,969	Saidi et al.	6-2001

WO 96/25918, Wood et al., Published 8-1996

US 2003/0073676, Biggadike et al., Published 4-2003

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 17, 19-24, 28-44, 47, 49-61, 64-67, 69, and 71-81 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Wiedmann et al. (US 5,747,001) in view of Saidi et al. (US 6,241,969).

Applicant's Invention

Applicant claims a sterile filterable composition comprising a) an aqueous dispersion medium; b) fluticasone particles and c) at least one surface stabilizer absorbed on the surface of the fluticasone particles. Applicant claims the dispersion is sterilized by filtration through a 0.2 μm filter. Applicant claims a method of making a fluticasone composition. Applicant also claims a method of treating a subject in need of either symptomatic or prophylactic treatment with a sterile particulate fluticasone composition.

Determination of the scope of the content of the prior art (MPEP 2141.01)

Wiedmann et al. teach an aerosol comprising droplets of an aqueous dispersion of nanoparticles, said nanoparticles comprising insoluble beclomethazone particles having a surface modifier on the surface thereof. There is also disclosed a method for making the aerosol and methods for treatment using the aerosol (Abstract). Wiedmann

et al. teach the aerosols of the present invention are particularly useful in the treatment of respiratory related illnesses. Wiedmann et al. teach that beclomethazone is particularly useful in the treatment of seasonal or perennial rhinitis and is also indicated for the relief of the symptoms of seasonal or perennial allergic and non-allergic (vasomotor) rhinitis (col. 2, lines 66-67-col. 3, lines 1-5). Wiedmann et al. teach that suitable surface modifiers can preferably be selected from known organic and inorganic pharmaceutical excipients. Wiedmann et al. further teach such excipients include various polymers, low molecular weight oligomers, natural products and surfactants. Preferred surface modifiers include nonionic and ionic surfactants. Wiedmann et al. teach tyloxapol is a preferred surface modifier and is a nonionic liquid polymer (col. 4, lines 52-67). Wiedmann et al. teach other specific surface modifiers that can be used in col. 3, lines 29-67-col. 4, lines 1-51). Wiedmann et al. teach examples include methylcellulose, vinyl acetate, polyvinyl pyrrolidone, gelatin, and casein (claims 32-37).

Wiedmann et al. teach the particles can be prepared in a method comprising the steps of dispersing beclomethazone in a liquid dispersion medium and applying mechanical means in the presence of grinding media to reduce the particle size of the beclomethazone to an effective average particle size of less than about 400 nm (claims 39-41, grinding). Wiedmann et al. teach the particles can be reduced in size in the presence of a surface modifier. Alternatively, the particles can be contacted with a surface modifier after attrition (col. 5, lines 65-67-col. 6, lines 1-7). Wiedmann et al. teach the he coarse beclomethazone selected can then be added to a liquid medium in which it is essentially insoluble to form a premix. Wiedmann et al. teach the premix can

be used directly by subjecting it to mechanical means to reduce the average particle size in the dispersion to less than 400 nm. Wiedmann et al. teach it is preferred that the premix be used directly when a ball mill is used for attrition. Wiedmann et al. teach that alternatively, the beclomethazone and, optionally, the surface modifier, can be dispersed in the liquid medium using suitable agitation, e.g., a roller mill or a Cowles type mixer, until a homogeneous dispersion is observed in which there are no large agglomerates visible to the naked eye (claim 42, homogenizing). It is preferred that the premix be subjected to such a premilling dispersion step when a recirculating media mill is used for attrition (col. 6, lines 17-40). Wiedmann et al. teach that another method of forming the desired nanoparticle dispersion is by microprecipitation. Wiedmann et al. teach this is a method of preparing stable dispersions of beclomethazone in the presence of a surface modifying and colloid stability enhancing surface active agent free of trace of any toxic solvents or solubilized heavy metal impurities by the following procedural steps: 1) Dissolving the beclomethazone in aqueous base with stirring, 2) Adding above #1 formulation with stirring to a surface active surfactant (or surface modifiers) solution to form a clear solution, and, 3) Neutralizing above formulation #2 with stirring with an appropriate acid solution. Wiedmann et al. teach the procedure can be followed by: 4) Removal of formed salt by dialysis or diafiltration and 5) Concentration of dispersion by conventional means. Wiedmann et al. teach this microprecipitation process produces dispersion of beclomethazone with Z-average particle diameter less than 400 nm (col. 9, lines 6-26). Wiedmann et al. teach an advantage of the microprecipitation is that unlike milled dispersion, the final product is

free of heavy metal contaminants arising from the milling media that must be removed due to their toxicity before product is formulated (col. 9, lines 57-60). Wiedmann et al. teach in preferred embodiments, the effective average particle size is less than about 300 nm and more preferably less than about 250 nm. Wiedmann et al. teach in some embodiments, an effective average particle size of less than about 100 nm has been achieved. Wiedmann et al. teach it is preferred that at least 95% and, more preferably, at least 99% of the particles have a particle size less than the effective average, e.g., 400 nm. Wiedmann et al. further teach that in some embodiments, essentially all of the particles have a size less than 250 nm (col. 10, lines 28-39).

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

Wiedmann et al. do not teach fluticasone particles or sterile filtration. It is for this reason Saidi et al. is added as a secondary reference.

Saidi et al. teach compositions containing corticosteroid compounds as active agents for the treatment of ailments and diseases of the respiratory tract, particularly the lungs, by way of nasal and pulmonary administration (Abstract). Saidi et al. teach the corticosteroid compositions of the present invention are preferably formulated with ethoxylated derivatives of vitamin E as the high-HLB surfactant component. An example of a preferred high-HLB surfactant from this class of surfactants is tocopheryl polyethylene glycol 1000 succinate ("TPGS") (col. 5, lines 40-42). Saidi et al. teach the particularly preferred are compounds include beclomethasone diproprionate, budesonide, and fluticasone propionate (col. 6, lines 27-30) (fluticasone). Saidi et al.

teach in example 1, col. 9, lines 65-67-col. 10, lines 1-16, the corticosteroid compositions were sterilized by passing them through a 0.22 micron sterile filter. Saidi et al. teach that for the treatment of bronchial constriction, the diluted corticosteroid composition is prepared as described above (sterile filtration and .2 μm filter). Saidi et al. teach the corticosteroid for such treatment is preferably beclomethasone dipropionate, betamethasone, budesonide, dexamethasone, flunisolide, fluticasone propionate, or triamcinolone acetonide (col. 9, lines 47-53).

Finding of prima facie obviousness
Rationale and Motivation (MPEP 2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of invention to combine the teachings of Wiedmann et al. and Saidi et al. and use fluticasone in the formulation. Wiedmann et al. teach aqueous dispersions of nanoparticles comprising beclomethazone particles that have a surface modifier on the surface used in the treatment of respiratory related illnesses. One skilled in the art at the time the invention was made would have been motivated to use fluticasone in the formulation because Saidi teach that fluticasone and beclomethasone are preferred compounds in the treatment of ailments and diseases of the respiratory system. Therefore, one skilled in the art at the time of invention would have been motivated to use fluticasone with a reasonable expectation of success as fluticasone and beclomethasone are functional equivalent glucocorticosteroids in the treatment of respiratory illnesses.

It would also have been obvious to one of ordinary skill in the art that the time the invention was made to use the sterile filtration technique as taught by Saidi et al. in the formulations and process of Wiedmann et al. since Wiedmann et al. teach filtration of nanoparticles of beclomethasone and tyloxapol, the preferred surface stabilizer of the instant application. One skilled in the art at the time the invention was made would have been motivated to implement sterile filtration of Saidi et al. instead of simple filtration of Wiedmann et al. because sterilization of formulations is beneficial to recipients.

Therefore, the claimed invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made because every element of the invention has been fairly suggested by the cited reference.

Claims 17, 19-24, 27-44, 47-61, 64-67, and 69-81 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Wood et al. (WO 96/25918) in view of Saidi et al. (US 6,241,969) in further view of Biggadike et al. (US 2003/0073676).

Applicant's Invention

Applicant claims a sterile filterable dispersion comprising a) an aqueous dispersion medium; b) fluticasone particles and c) at least one surface stabilizer absorbed on the surface of the fluticasone particles. Applicant claims the dispersion is sterilized by filtration through a 0.2 μm filter. Applicant claims a method of making a fluticasone composition. Applicant also claims a method of treating a subject in need of either symptomatic or prophylactic treatment with a sterile particulate fluticasone composition.

Determination of the scope of the content of the prior art (MPEP 2141.01)

Wood et al. teach an aerosol comprising droplets of an aqueous dispersion of nanoparticles wherein the nanoparticles comprise insoluble therapeutic or diagnostic agent particles having a surface modifier on the surface (page 2, lines 25-28). Wood et al. further teach a method of treating a mammal comprising the steps of forming an aerosol of an aqueous dispersion of nanoparticles, wherein the nanoparticles comprise insoluble therapeutic agent particles having a surface modifier on the surface and administering the aerosol to the respiratory system of the mammal (page 2, lines 35-36-page 3, lines 1-5). Wood et al. teach the aerosols are useful in the treatment of respiratory related illnesses such as asthma, emphysema, respiratory distress syndrome, chronic bronchitis, cystic fibrosis, and AIDS related pneumonia (conditions and method of treating). Wood et al. teach suitable therapeutic agents can be elected from a variety of known classes including anti-inflammatory agents and corticosteroids (page 4, lines 26-36). Wood et al. teach suitable surface modifiers can be selected from known organic and inorganic pharmaceutical excipients. Wood et al. teach the excipients include various polymers, low molecular weight oligomers, natural products and surfactants. Wood et al. teach preferred surface modifiers include nonionic and ionic surfactants (page 6, lines 2-5). Wood et al. teach representative examples of surface modifiers include casein, lecithin, gum acacia, polyethylene glycols, PVP (page 6, lines 6-21). Wood et al. teach preferred surface modifiers include tyloxapol (tyloxapol) (page 6, lines 22-36). Wood et al. teach that two or more surface modifiers can be used in combination (page 7, lines 33-34) (at least 2 surface stabilizers).

Wood et al. teach the particles can be prepared in a method comprising the steps of dispersing a therapeutic or diagnostic agent in a liquid dispersion medium and applying mechanical means in the presence of grinding media to reduce the particle size of the therapeutic agent to an effective average particle size of less than about 400 nm. Wood et al. teach the particles can be reduced in size in the presence of a surface modifier (page 9, lines 30-32-page 10, lines 1-5) (method of making, grinding). Wood et al. teach the surface modifier is present in an amount of 0.1-90%, preferably 20-60% by weight based on the total weight of the dry particle (page 17, lines 10-11) (weight ratios). Example 1 teaches the preparation and use of beclomethasone nanoparticles (page 18, lines 17-36).

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

Wood et al. do not teach fluticasone particles or sterile filtration. It is for this reason Saidi et al. and Biggadike et al. are added as a secondary references.

The teachings of Saidi et al. are incorporated herein by reference and are therefore applied in the instant rejection as discussed above.

Biggadike et al. teach a pharmaceutical formulation comprising an aqueous carrier liquid having dissolved therein an ester of fluticasone or a solvate as medicament and a solubilizing agent for assisting the solubilization of the medicament in the aqueous carrier liquid. Biggadike et al. teach that fluticasone esters are quite insoluble in water (page 2, paragraph 15). Biggadike et al. teach that the solubility of fluticasone esters can be increased by dissolution in the aqueous carrier liquid of a hydroxyl containing organic co-solvating agent or of phosphatidiyl choline (page 2,

paragraph 16). Biggadike et al. further teach the preferred surfactant to be used as the solubilizing agent is tyloxapol (page 2, paragraph 21). Biggadike et al. teach that the formulations of the inventions may be employed for rectal, aural, otic, topical or parenteral administration or administration by inhalation for the treatment of other local inflammatory conditions such as dermatitis, asthma, and COPD (page 4, paragraph 56) (conditions and methods of administration).

Finding of prima facie obviousness
Rationale and Motivation (MPEP 2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of invention to combine the teachings of Wood et al., Saidi et al., and Biggadike et al. and use fluticasone in the formulation. Wood et al. teach the preparation, method of making and method of using aqueous dispersion of nanoparticles wherein the nanoparticles comprise insoluble therapeutic or diagnostic agent particles having a surface modifier on the surface. Wood et al. specifically teach that preferred examples of agents that can be used in the preparation include anti-inflammatory and corticosteroids, of which drug class fluticasone belongs. In addition, the working example uses beclomethasone in the preparation of the nanoparticles. One skilled in the art at the time the invention was made would have been motivated to use fluticasone in the formulation because Saidi teach that fluticasone and beclomethasone are preferred compounds in the treatment of ailments and diseases of the respiratory system. In addition, Biggadike et al. teach that the preferred surface stabilizer, tyloxapol, is a preferred surfactant used to solubilize fluticasone and fluticasone esters. Therefore, one skilled in the art at the time of

invention would have been motivated to use fluticasone in the formulation with a reasonable expectation of success as fluticasone and beclomethasone are functional equivalent glucocorticosteroids in the treatment of respiratory illnesses and fluticasone is a member of two of the preferred drug classes that can be used in making the aerosol.

It would also have been obvious to one of ordinary skill in the art that the time the invention was made to use the sterile filtration technique as taught by Saidi et al. in the formulations and process of Wood et al. since Wood et al. teach filtration of nanoparticles of beclomethasone and tyloxapol, the preferred surface stabilizer of the instant application. One skilled in the art at the time the invention was made would have been motivated to implement sterile filtration of Saidi et al. instead of simple filtration of Wood et al. because sterilization of formulations is beneficial to recipients.

Therefore, the claimed invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made because every element of the invention has been fairly suggested by the cited reference.

(10) Response to Argument

Appellant argues that "there is no teaching or suggestion that Wiedmann's composition is suitable for sterile filtration". Appellant continues that "there is no teaching that fluticasone aerosol compositions can be sterile filtered through a 0.2μm filter and that Wiedmann teaches particle size of less than 400 nm". This is not persuasive because Wiedmann et al. disclose that in preferred embodiments, the

effective average particle size is less than 300 nm and more preferably less than about 250 nm. Wiedmann et al. further disclose that in some embodiments, an effective average particle size of less than about 100 nm has been achieved. Wiedmann et al. disclose in some embodiments, essentially all of the particles have a size less than 250 nm. The skilled artisan would find it obvious that with the teaching that some embodiments have an average particle size of less than about 100 nm or particle sizes less than 250 nm that many of the particles will fall within the range of 200 nm and that these particles would easily pass through a sterile filter with a 0.2 µm filter. Within these ranges, 250 nm particles and 100 nm particles, the skilled artisan would find it obvious to optimize the particle size to make it small enough to pass through a 0.2 µm sterile filter.

In response to Appellant's argument that Wiedmann et al. provides no teaching that fluticasone aerosol compositions can be sterile filtered through a 0.2 µm filter, Wiedmann et al., disclose the use of dispersions of beclomethasone particles that have a surface stabilizer absorbed on the surface of the particles dispersed in an aqueous medium. Wiedmann et al. also disclose that the grinding media is separated from the milled particulate product using conventional separation techniques such as filtration (col. 7, lines 18-21) and simple filtration (col. 8, lines 47-52). Saidi et al. was relied on as the secondary reference to teach the primary drug, fluticasone, and sterile filtration as the specific filtration technique. One skilled in the art at the time of invention would have been motivated to use fluticasone as the primary drug because Saidi et al. disclose that fluticasone and beclomethasone are both corticosteroids, functional equivalents, that

are preferred compounds in the treatment of ailments and diseases of the respiratory system. Therefore, the skilled artisan would have found it obvious to try another corticosteroid, particularly fluticasone, in the compositions disclosed by Wiedmann et al. that have particle sizes that are as small as 100 nm, small enough to be sterile filtered through a 0.2 μm filter because these compositions are both corticosteroids that have similar properties.

Appellant argues that "it is impossible to apply Saidi's sterile filtration technique to Wiedmann's composition". Appellant continues that "Saidi applies sterile filtration to drug solutions rather than dispersions". Appellant argues that "one skilled in the art would have understood that a solution can easily pass a 0.22 micron filter while a dispersion may cause the filter to clog if the particles in the dispersion are not sufficiently small". This argument is not persuasive because Wiedmann et al. disclose that in some embodiments, an effective average particle size of less than about 100 nm has been achieved. Wiedmann et al. also disclose in some embodiments, essentially all of the particles have a size less than 250 nm. The skilled artisan would find it obvious that with the teaching that some embodiments have an average particle size of less than about 100 nm or particle sizes less than 250 nm that many of the particles will fall within the range of 200 nm and that these particles would easily pass through a sterile filter with a 0.2 μm filter. Within these ranges the skilled artisan would find it obvious to optimize the particle size to make it small enough to pass through a 0.2 μm filter. In addition, Applicant's claim 23 and claims that depend from claim 23 are drawn to a composition, not a dispersion. Therefore, any type of formulation, i.e. solutions, that

comprises particles of fluticasone and at least one surface stabilizer absorbed on the surface of the fluticasone will read on the claims and would easily pass through a sterile filter with a 0.22 micron filter.

Appellant argues that "the examiner has improperly assigned a nexus between Wiedmann's filtration step and Saidi's sterile filtration". Applicant argues that "Wiedmann et al. used the filtration step to separate larger particles from smaller ones in a separation technique". Applicant continues that "the sterile filtration of Saidi et al. is used to remove microorganisms in a sterilization technique". This is not persuasive because as noted in the previous Office Actions, Wiedmann et al. disclose several techniques that can be used to separate and form the nanoparticles. One technique disclosed is microprecipitation. Wiedmann et al. disclose this is a method of preparing stable dispersions of beclomethazone in the presence of a surface modifying and colloid stability enhancing surface active agent free of trace of any toxic solvents or solubilized heavy metal impurities by the following procedural steps: 1) Dissolving the beclomethazone in aqueous base with stirring, 2) Adding above #1 formulation with stirring to a surface active surfactant (or surface modifiers) solution to form a clear solution, and, 3) Neutralizing above formulation #2 with stirring with an appropriate acid solution. Wiedmann et al. disclose the procedure can be followed by: 4) Removal of formed salt by dialysis or diafiltration and 5) Concentration of dispersion by conventional means (col. 9, lines 6-26). Wiedmann et al. disclose an advantage of the microprecipitation is that unlike milled dispersion, the final product is free of heavy metal contaminants arising from the milling media that must be removed due to their toxicity

before product is formulated (col. 9, lines 57-60). Step 4 of the process is the removal of salt by dialysis or diafiltration. This technique provides a removal of contaminants, a sterilization of the particles. As such, the skilled artisan would find it obvious to use any of the techniques disclosed by Wiedmann et al. to form the particles, particularly microprecipitation that will also filter out contaminants. In addition, some of the particles that are disclosed by Wiedmann et al. have particles sizes of 100 nm and 250 nm which would easily pass through the sterile filter of .22 microns disclosed by Saidi et al.

Appellant argues that "Wood et al. is directed toward aerosol dispersions with particle size less than 400 nm, not 200 nm". Appellant continues that "Wood et al. provide no evidence that Wood's aerosol compositions are suitable for sterile filtration or an indication that Saidi's sterile filtration technique can be applied to Wood's composition". This argument is not persuasive because Wood et al. disclose that in some embodiments, an effective average particle size of less than about 100 nm has been achieved (page 16, lines 29-30). The skilled artisan would find it obvious with the teaching that in some embodiments an average particle size of less than about 100 nm has been achieved that these particles would easily passes through a sterile filter with a 0.2 μm filter, the filter size disclosed by Saidi et al.

In response to Appellant's argument that Wood et al. provides no evidence that Wood's aerosol compositions are suitable for sterile filtration or an indication that Saidi's sterile filtration technique can be applied to Wood's composition, Wood et al. disclose an aqueous dispersion of nanoparticles wherein the nanoparticles comprise insoluble therapeutic or diagnostic agent particles having a surface modifier on the surface. Wood

et al. also disclose that several methods of producing the dispersions can be used, including filtration (page 12, line 2-5) and precipitation (page 14, lines 30-36-page 15, lines 1-36). Saidi et al. was relied on as the secondary reference to teach the primary drug, fluticasone, and sterile filtration as the specific filtration technique. Wood et al. disclose that in some embodiments an effective average particle size of less than about 100 nm has been achieved (page 16, lines 29-30). The skilled artisan would find it obvious with this teaching, some embodiments having an average particle size of less than about 100 nm, would easily pass through a sterile filter with a 0.2 μm filter, the sterile filter size as disclosed in Saidi et al.

Appellant argues that "Wood et al. teach filtration for separation instead of sterilization". In response to Appellant's argument, Wood et al. disclose several techniques that can be used to separate and form the nanoparticles dispersion. One technique disclosed it microprecipitation (page 14, lines 30-36-page 15, lines 1-36). Wood et al. disclose that this is a method of preparing stable dispersions of therapeutic and diagnostic agents in the presence of a surface modifying and colloid stability enhancing surface active agent free of trace of any toxic solvents or solubilized heavy metal impurities by the following procedural steps: 1) Dissolving the therapeutic and diagnostic agents in aqueous base with stirring, 2) Adding above #1 formulation with stirring to a surface active surfactant (or surface modifiers) solution to form a clear solution, and, 3) Neutralizing above formulation #2 with stirring with an appropriate acid solution. Wood et al. disclose the procedure can be followed by: 4) Removal of formed salt by dialysis or diafiltration and 5) Concentration of dispersion by conventional

means. Wood et al. disclose an advantage of the microprecipitation is that unlike milled dispersion, the final product is free of heavy metal contaminants arising from the milling media that must be removed due to their toxicity before product is formulated. Step 4 of the process is the removal of salt by dialysis or diafiltration. This technique provides a removal of contaminants, a sterilization of the particles. As such, the skilled artisan would find it obvious to use any of the techniques disclosed by Wood et al. to form the particles, particularly microprecipitation that will also filter out contaminants. In addition, some of the particles that are disclosed by Wood et al. have particles sizes of 100 nm which would easily pass through the sterile filter of .22 microns disclosed by Saidi et al.

Appellant argues that "Biggadike in combination with Wood et al. and Saidi et al. fails to render the claimed invention obvious". Appellant continues that "the examiner failed to establish why one skilled in the art would have any reason to select tyloxapol as a surface stabilizer, which absorbs on the surface of fluticasone particles instead of a solubilizer". This argument is not persuasive because Wood et al. disclose that tyloxapol may function as a surface modifier, as a stabilizer, and/or as a dispersant (solubilizer) with nanoparticles. Wood et al. further disclose the tyloxapol may serve all three functions. As noted in the previous office actions, Biggadike et al. disclose that the preferred surface stabilizer of the instant application, tyloxapol, is a preferred surfactant used to solubilize fluticasone and fluticasone esters. With the teaching of Wood et al. that tyloxapol can be used as a surface stabilizer, surface modifier, and a dispersant (solubilizer); the skilled artisan would have found it obvious to use tyloxapol, the preferred surfactant for the solubilization of fluticasone, as a surface modifier for

fluticasone. In addition, Wood et al. disclose that tyloxapol is a useful nonionic surface active agent in a lung surfactant composition. As such, the skilled artisan would find it obvious to try tyloxapol as a surface modifier for fluticasone, a therapeutic agent used to treat respiratory ailments, because tyloxapol is a compatible dispersant or solubilizer for fluticasone that as taught by Wood et al. can also be used as a surface modifier.

It is maintained that the combination of the references cited render instant claims obvious.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Johann R. Richter/

Supervisory Patent Examiner, Art Unit 1616

Conferees:

/Andriae M. Holt/

Patent Examiner, Art Unit 1616

/Michael G. Hartley/

Supervisory Patent Examiner, Art Unit 1618